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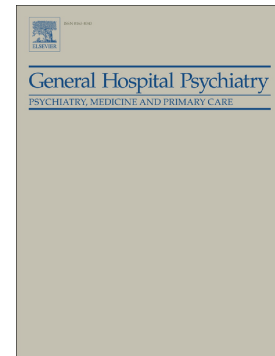
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## Accepted Manuscript

Diseases of the pancreas and suicide mortality: A nationwide nested case-control study among patients with mental health disorders in Taiwan

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**Diseases of the pancreas and suicide mortality: A nationwide nested case-control study among patients with mental health disorders in Taiwan**

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# Vincent Chin-Hung Chen contributed equally to Hong-Ming Chen

**Short running title:** Diseases of the pancreas and suicide mortality

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**Abstract**

**Objective:** Diseases of the pancreas, especially pancreatitis, have been implicated as possible risk factors for psychiatric illnesses, such as depression and anxiety disorder. This nested case-control study aimed to investigate the association between diseases of the pancreas and completed suicide in a psychiatric population-based study.

**Methods:** The case group comprised 6,568 completed suicides (ICD-9: E950-E959, E980-989) patients from the national mortality database between January 1, 2002 and December 1, 2010. These cases were compared with 6,568 gender-, age-, residence-, and insurance premium-matched controls. Both suicide and non-suicide study patients were drawn from a group with previous psychiatric diagnoses. The risk of suicide among patients with diseases of the pancreas was analyzed using a conditional logistic regression model that controlled for alcohol-related disorder, drug dependence, schizophrenia, depressive disorder, bipolar disorder, anxiety disorder, Charlson comorbidity score, and outpatient visits.

**Results:** Disease of the pancreas was an independent risk factor for psychiatric patients who had completed suicide when adjusted for clinical and other comorbid factors. Among these covariates, alcohol-related disorders partially mediate the suicide risk among patients with disease of the pancreas, and mental disorders may not mediate this suicide risk.

**Conclusions:** Diseases of the pancreas were associated with increased risk of completed suicide after controlling for potential confounding factors.

**Key words:** Diseases of the pancreas, pancreatitis, suicide, mental disorders

## Introduction

Diseases of the pancreas, primarily acute and chronic pancreatitis, are common gastrointestinal causes of hospital admission [1]. Besides the financial cost of admission, chronic pancreatitis also reduces patient quality of life [2]. There are multiple causes for pancreatitis, including alcohol intake, hyperlipidemia, obstruction of pancreatic duct, trauma, medication use, and autoimmune disease. Acute pancreatitis is an acute abdominal disorder which usually needs hospital admission and has an overall mortality rate of 2–5% [3]. Chronic pancreatitis, a consequence of repeated acute pancreatitis or injury of the pancreas, is a progressive and debilitating disease, which usually needs further pain control.

Current studies indicate that patients with pancreatitis, no matter whether acute or chronic, might have poor mental health. One review which included 16 studies showed that quality of life declined after acute pancreatitis [4]. In patients with chronic pancreatitis, quality of life also declined, with especially the problem of pain [5]; they also suffered from depression, anxiety, or addiction that needed to be managed [6]. In addition, mental disorders may also interact with pancreatic disorders and worsen them. A report indicated that concomitant mental disorder predicted hospital readmissions of patients with acute and chronic pancreatitis [7]. Comorbid psychological problem or psychiatric disorder should be also part of the treatment target for diseases of the pancreas.

Mental disorders, especially depressive disorders, have been known to be associated with risk of suicide [8-10]. Thus, we hypothesized that diseases of the pancreas, especially pancreatitis with known consequences for mental health, had higher risk of suicide too. The rate of suicide in pancreatic cancer increased significantly [11], but knowledge about the suicide risk of diseases of the pancreas is limited. A 5-year nationwide study in Denmark reported mortality and the causes of death for patients with chronic pancreatitis [12]. They indicated that patients with chronic pancreatitis, compared with controls, have a significantly higher mortality rate, more cancer incidence, more cancer-associated death, and a higher suicide rate. However, no further covariates were analyzed in that study.

The present study aimed to investigate the association between diseases of the pancreas and suicide mortality among a population with mental disorders through a nationwide database study. We hypothesized that patients with diseases of the pancreas have a higher risk of completed suicide. We also explored various covariates that were associated with diseases of the pancreas and suicide, such as mood disorders and alcohol use disorders [13, 14] to clarify if they can affect this association.

## Method

### Study subject and control definition

The government of Taiwan started a nationwide health insurance program on March 1, 1995. It also developed a National Health Insurance Research Database (NHIRD) for research usage [15]. By December 2010, 23.074 million people were enrolled nationwide, with a coverage rate of 99.6%. In this study, we enrolled patients who had a psychiatric diagnosis (International Classification of Diseases (ICD)-9: 290-319) during the period 2002-2010. A diagnosis was defined as having a medical claim with the relevant diagnostic code on one occasion through inpatient services or on multiple occasions spread over at least one year through outpatient services; 2,329,989 people were enrolled (figure 1). We designed a nationwide nested case-control study. The nationwide mortality database of those aged 15 years and above was provided by the Department of Health of the Executive Yuan of Taiwan for the years 2002-2010. Since suicide mortality statistics are usually underestimated, and the most commonly misclassified category is death from undetermined causes, suicide deaths were defined in this study as those coded E950-E959 and E980-E989 according to the ICD-9. Among people with a diagnosis of psychiatric illness, there were 6,568 completed suicides during the period 2002–2010 in Taiwan, including 4,156 male suicides and 2,412 female suicides, with a male-to-female ratio of 1.9. These cases were compared with 6,568 controls matched on sex-, age-, residence-, and insurance premium (a proxy indicator of economic status) also drawn from those with a diagnosis of psychiatric illness. Both suicide and non-suicide study patients were hence drawn from a group with previous psychiatric diagnoses.

[Insert Figure 1 here]

### Ethics Statement

The Institutional Review Board (IRB) of the Chang Gung Memorial Hospital approved this study which was conducted in Taiwan. The patients were not required to give written consent for the study because the NHIRD and mortality database consists of de-identified secondary data used for research purposes, and the IRB gave a formal written waiver of the need for consent.

### Statistical analysis

Diseases of the pancreas (ICD-9: 577.X) were analyzed using a conditional logistic regression model that controlled for mental disorders (schizophrenia (ICD-9: 295.XX), depressive

disorders (ICD-9: 296.2X, 296.3X, 300.4, and 311), bipolar disorders (ICD-9: 296.0, 296.4, 296.5, 296.6, 296.7, 296.80 or 296.89), anxiety disorders (ICD-9: 300.0, 300.01, 300.02, 300.2, 300.21, 300.23, 300.3)), alcohol-related disorders (ICD-9: 291, 303.0, 303.9, 305.0, 571.0, 571.1, 571.2, or 571.3), drug dependence (substance apart from alcohol, ICD-9:304), and general health condition (Charlson comorbidity score and outpatient visits). All of the potential comorbid diseases and Charlson comorbidity score were defined using outpatient and inpatient diagnosis before the index date, and outpatient visits were calculated by one-year medical claims before the index date. The index date was defined as the date of suicide for the case and assigned to their matched control. The odds-ratio (OR), which indicates the association between diseases of the pancreas and suicide, was estimated. First, we performed univariate conditional logistic regression to reveal the unadjusted association between each covariate and suicide. Second, we performed multivariable regression, including all previous covariates except alcohol-related disorder (model 1). Finally, we included all study covariates including alcohol-related disorders for further adjustment to confirm if diseases of the pancreas contributed to risk of suicide independently (model 2). The model was tested using the total group of patients initially and then using subgroups according to gender and age (15-44, 45-64 and  $\geq 65$  years) (table 3). Analyses were carried out using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

## Results

### Clinical characteristic of suicide and non-suicide group

In total, 6,568 suicide cases and 6,568 non-suicide matched controls were included among psychiatric illness population. Table 1 shows the demographic and clinical characteristics of suicide cases and non-suicide controls. Because of the exact matching, there was no difference in gender, age, residence (rural, urban), and insurance premium (a proxy indicator of economic status). In suicide cases, there were more diseases of the pancreas, alcohol-related disorders, drug dependence, schizophrenic disorders, depressive disorders, bipolar disorders, and anxiety disorders (all  $P < 0.001$ ). Compared with the control group, suicide cases had higher Charlson comorbidity score  $\geq 4$  (26.42% vs. 19.49%) and more frequent outpatient visits ( $\geq 31$  times in one year before the index date, 45.37% vs. 26.33%)

[Insert Table 1 here]

### Unadjusted (univariate) analysis

Diseases of the pancreas were associated with suicide risk (OR = 2.66, 95% CI=2.08-3.38,



$P < 0.001$ ). Among other study covariates, alcohol-related disorders, drug dependence, schizophrenic disorders, depressive disorders, bipolar disorders, anxiety disorders, Charlson comorbidity score, and outpatient visits were also associated with suicide risk (Table 2).

[Insert Table 2 here]

### **Adjusted analysis**

We included all study covariates except alcohol-related disorders in model 1 (Table 2), and the strength of association between diseases of the pancreas and suicide risk ( $OR = 2.67$ ) was similar to the unadjusted value ( $OR = 2.66$ ). All of the other study covariates, drug dependence, schizophrenic disorders, depressive disorders, bipolar disorders, anxiety disorders, Charlson comorbidity score, and outpatient visits were also associated with suicide risk independently after adjustment (Table 2).

In model 2, we adjusted for all covariates including alcohol-related disorders (Table 2). The suicide risk of each covariate was similar to the result in model 1. However, the association of diseases of the pancreas to suicide risk decreased from  $OR = 2.67$  to  $1.60$ .

### **Stratified analysis of diseases of the pancreas with suicide**

In Table 3, we further analyzed by gender or age groups (15-44, 45-64 and  $\geq 65$  years) to determine any high-risk subgroups. In unadjusted analysis, both gender and all age subgroups showed an association with suicide risk. After initial adjustment (model 1), the result was similar to the unadjusted analysis. After further adjustment of alcohol-related disorder (model 2), the risk in males significantly decreased ( $OR = 2.59$  to  $1.46$ ). In contrast, the risk decreased less in the female group than males ( $OR = 2.60$  to  $2.32$ ). In model 2, the risk of suicide also significantly decreased in aged 15-44 ( $OR = 3.63$  to  $1.74$ ) and aged 45-64 ( $OR = 2.25$  to  $1.35$ ), but was steady in aged  $\geq 65$  ( $OR = 1.93$  to  $1.70$ ).

[Insert Table 3 here]

### **Discussion**

In this nested case-control study, we found that diseases of the pancreas were associated with suicide risk in initial unadjusted analysis ( $OR: 2.66$ ,  $CI = 2.08-3.38$ ). After adjustment for other covariates including mental disorders, general physical condition, and other substance dependence except for alcohol (model 1), the association changed little ( $OR = 2.66$  to  $2.67$ ). After adjustment

for alcohol-related disorder (model 2), the association between pancreatic disorder and suicide declined but was still independent (OR: 2.67 to 1.60).

### **Diseases of the pancreas and suicide risk**

Diseases of the pancreas, primarily acute or chronic pancreatitis, were associated with higher suicide risk in our report. We focus on a psychiatric group and tried to clarify if mental disorders or alcohol use mediated this association. The result showed that alcohol use but not mental disorders partially mediate this suicide risk. According to past research, we had known that completed suicide in Taiwan is associated with five major risk factors (loss event, suicidal behavior in first-degree relatives, major depressive episode, emotionally unstable personality disorder and substance dependence) [10]. Patients with acute/chronic pancreatitis may have experienced more loss events or had a more dominant family history of suicide. We should also consider the suffering from pain or declining quality of life, which may potentially contribute to the increased suicide risk [4, 5].

### **The role of mental disorders**

Depression is well known as a major risk for completed suicide [8, 10]. Comorbid mental disorder also contributes to the risk of completed suicide [9]. When investigating the suicide risk among diseases of the pancreas, the influence of comorbid depression and other mental disorders should always be considered. A cross-sectional study in South Carolina found that depressive symptoms are common among patients with non-alcohol-related chronic pancreatitis, and it may be a risk factor associated with increased pain and decreased quality of life [16]. Jeppe et al. also indicated that the relationship between chronic pancreatitis, depression and substance use disorders, seems to be circular and multiplicative [13]. Our suicide cases had higher prevalence of mental disorder than the control group: schizophrenia (8.57% with 2.45%,  $p<0.001$ ), depression (42.89% with 11.88%,  $p<0.001$ ), bipolar disorders (5.85% with 1.23%,  $p<0.001$ ), anxiety disorders (34.9% with 27.42%,  $p<0.001$ ). Initially, in our unadjusted analysis, mental disorders (OR=1.45-5.87) and diseases of the pancreas (OR=2.66, CI=2.08-3.38) were associated with suicide risk. When we adjusted pancreatic disorder with mental disorders except for alcohol use disorder in model 1, the risk of suicide among patients with pancreatic disorder changed little. Thus we supposed that comorbid depression or other mental disorders does not mediate or moderate suicide risk among patients with diseases of the pancreas.

### **The role of Alcohol-related disorder**

A recent meta-analysis showed that alcohol disorder was a risk factor for suicidal ideas, suicide attempt, or completed suicide [17]. It was also known that alcohol use was associated with acute or chronic pancreatitis [18, 19]. Thus we proposed that alcohol use might be a mediator for suicide risk among patients with pancreatic disorder. In our initial unadjusted analysis, pancreatic disorder (OR=2.66, CI=2.08-3.38) and alcohol-related disorder (OR= 3.44, CI= 2.97-3.99) were both associated with suicide risk. After adjustment for all covariates including alcoholic disorder (model 2), alcoholic disorder still increased the risk of suicide (OR= 3.35, CI=2.81-4.00). The suicide risk among patients with pancreatic disorder decreased but it was still statistically significant (OR= 2.66 to 1.6). This suggests that alcohol use disorder partially mediates the suicide risk among pancreatic patients with psychiatric illness.

### **The role of general physical condition**

Disease of the pancreas, especially chronic pancreatitis, is a chronic disease that causes suffering and is disabling [13]. One study focusing on patients with non-cancer pain found that it increased the risk of suicide [20]. Qin et al. found that suicide risk in physically ill people varies by their psychiatric comorbidity [21]. We used two indexes to evaluate the general physical condition of our cases and controls: the Charlson comorbidity scores, and the number of outpatient visits for any reason in one year before the index date. In our suicide cases, there is a higher rate of people with high Charlson comorbidity score ( $\geq 4$ ) (26.42% with 19.49%,  $p < 0.001$ ), and also a higher rate of people with more outpatient visits ( $\geq 31$  times in one year before the index date) (45.37% with 26.33%,  $p < 0.001$ ). After adjustment for all covariates (model 2), we found that outpatient visits could predict suicide risk (OR=2.7 in the most frequent group), but not Charlson comorbidity scores. Frequent outpatient visiting might imply psychological or physical conditions that deserve more attention for suicide prevention among these people.

### **Patients with diseases of the pancreas and suicide: who has higher risk?**

In table 3, we further analyzed the effects of demographic variables on suicide risk among patients with diseases of the pancreas. After controlling for alcohol use, we found suicide risk decreased in people with male gender (OR= 2.59 to 1.46), adult age (OR= 3.63 to 1.74) or middle age (OR= 2.25 to 1.35). In contrast, the suicide risk of female (OR=2.60 to 2.32) and the elder group (OR=1.93 to 1.70) did not decrease so much. This result indicated that patients with diseases of the pancreas in male gender or non-elder age were vulnerable to alcohol-induced suicide risk. Indeed, epidemiological data support that these people have a higher rate of alcohol use. In a large study of alcohol consumption in China, it showed higher rate of abstainers in female than in male

(63.6% with 20.3%); and higher rate of abstainers in older people (age 70-79: 33.6%) than younger adult (age 30-49: 14.2-15.7%) or middle age (age 50-59: 19.75%) [22] . This finding helps us to focus our effort about suicide prevention on such a subgroup: pancreatic disorder in male gender and younger age with drinking problems.

### **Strength and limitation**

To our knowledge, this is the first study using a nationally representative sample with a nested case-control design to clarify the association of diseases of the pancreas (in particular pancreatitis) and suicide risk with control for various covariates including mental disorders, substance use, and general physical condition. In a previous study in Denmark [12], they observed a higher suicide rate among chronic pancreatitis than the control group (hazard ratio=3.5, 95% CI=2.6-4.7). However, the consideration of further confounding factors was absent in that study. In our study, we tried to test the influence of various covariates, including age, gender, residence, economic status, comorbid mental disorder, general physical condition, alcoholic disorder, and other substance dependence. Nonetheless, there are also some limitations to our study. First, the validity of physical or mental diagnosis was limited in a nationwide database, and some bias may be inevitable. Second, our study presents an observational finding in Taiwan, for a specific psychiatric group, which may not be the same in other areas in the world with different types of diseases of the pancreas, different prevalence of mental disorders, different causes of suicide, and a different drinking culture. Third, we could not include further detailed data known to be associated with suicide in Taiwan, such as personality disorder, family history, and recent psychosocial stress [10].

### **Conclusion**

This study suggests that diseases of the pancreas increase the risk of suicide independently. The strategy of suicide prevention among these patients with diseases of the pancreas may be focused on not only alcohol use disorder (a partial mediator) but also the suffering from diseases of the pancreas such as pain or declining quality of life.

## Abbreviations

NHIRD, National Health Insurance Research Database; ICD, International Classification of Diseases; IRB, Institutional Review Board; OR, odds ratio

## Declarations

### *Ethics Approval and Consent to Participate*

Not applicable

### *Author Contribution*

Study concept and design: HM Chen, VCH Chen, CP Tsai

Acquisition of data: VCH Chen, CP Tsai

Analysis and interpretation of data: VCH Chen, CP Tsai, ME Dewey

Drafting of the manuscript: HM Chen, VCH Chen, CP Tsai, ME Dewey

Critical revision of the manuscript for important intellectual content: TN Wang, ML Lu, YJ Huang, ME Dewey, JKW Lee

Statistical analysis: CP Tsai

Obtained funding: VCH Chen

Technical or material support: TN Wang, ML Lu, YJ Huang

Study supervision: VCH Chen, CP Tsai

### *Competing interests*

The authors have no financial interests or potential conflicts of interest to declare.

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Figure 1 Flow chart of data collection in this study

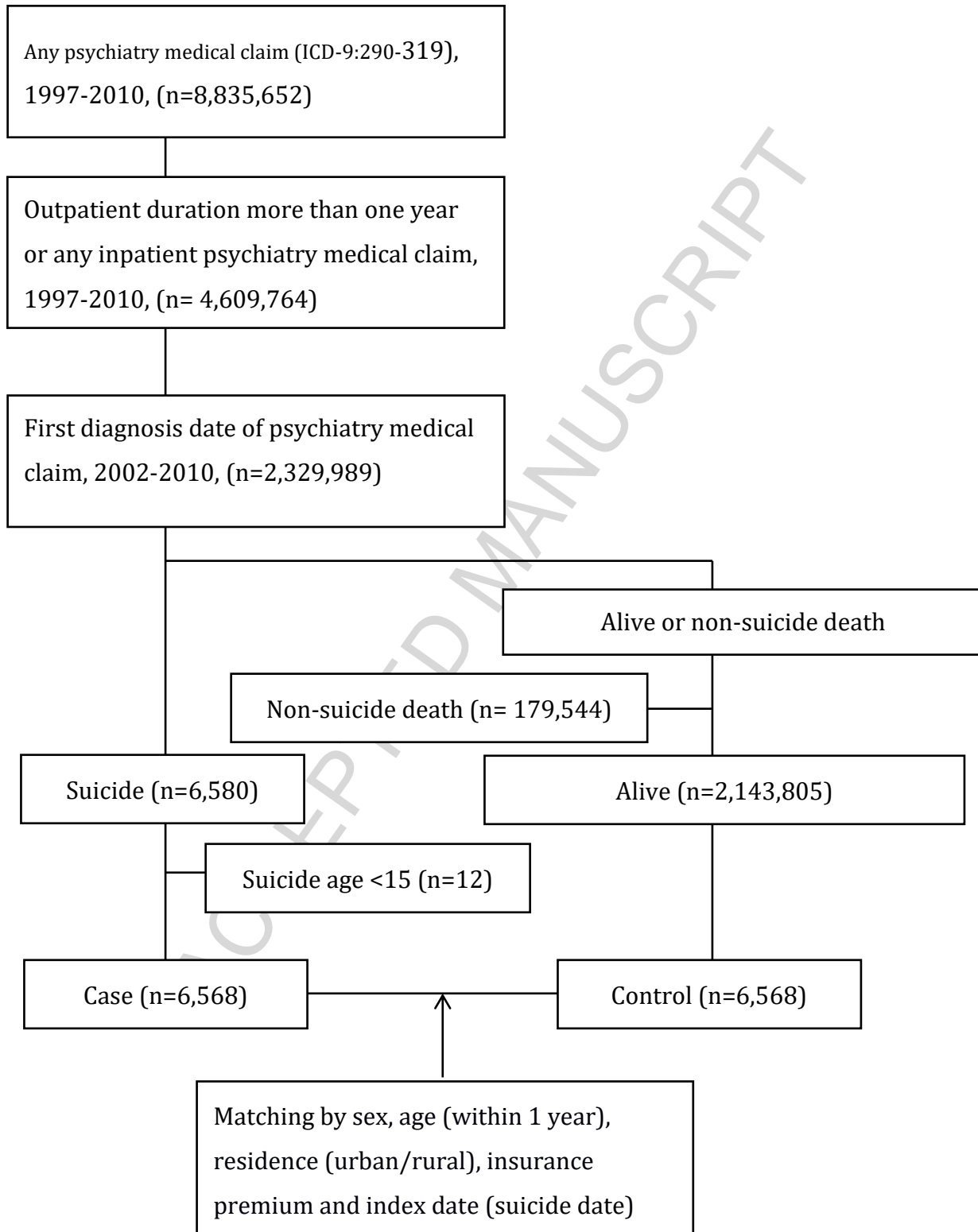


Table 1. Demographic and clinical characteristic of suicide and non-suicide after exact matching, Taiwan, 2002-2010.

| Characteristic                               | Suicide, n=6,568 (%) | Non-suicide, n=6,568 (%) | P value |
|--|----------------------|--------------------------|---------|
| Gender                                       |                      |                          |         |
| Male   | 4156 (63.28)         | 4156 (63.28)             | >0.99   |
| Female                                       | 2412 (36.72)         | 2412 (36.72)             |         |
| Age at index date, year                      |                      |                          |         |
| 15-44  | 3093 (47.09)         | 3093 (47.09)             | >0.99   |
| 45-64  | 2156 (32.83)         | 2156 (32.83)             |         |
| ≥65  | 1319 (20.08)         | 1319 (20.08)             |         |
| Residence                                    |                      |                          |         |
| Rural  | 1689 (25.72)         | 1689 (25.72)             | >0.99   |
| Urban  | 4879 (74.28)         | 4879 (74.28)             |         |
| Insurance premium, NTD <sup>a</sup>          |                      |                          |         |
| Fixed premium and dependent                  | 2188 (33.31)         | 2188 (33.31)             | >0.99   |
| Less than 19,999                             | 2560 (38.98)         | 2560 (38.98)             |         |
| 20,000-39,999                                | 1532 (23.33)         | 1532 (23.33)             |         |
| ≥40000                                       | 288 (4.38)           | 288 (4.38)               |         |
| Medical & mental diseases <sup>b</sup> , yes |                      |                          |         |
| Pancreatic disorder                          | 247 (3.76)           | 98 (1.49)                | <.001   |
| Alcohol-related disease                      | 835 (12.71)          | 276 (4.2)                | <.001   |
| Drug-dependent                               | 191 (2.91)           | 48 (0.73)                | <.001   |
| Schizophrenia                                | 563 (8.57)           | 161 (2.45)               | <.001   |
| Depression disorder                          | 2817 (42.89)         | 780 (11.88)              | <.001   |
| Bipolar disorder                             | 384 (5.85)           | 81 (1.23)                | <.001   |
| Anxiety disorder                             | 2292 (34.9)          | 1801 (27.42)             | <.001   |
| Charlson comorbidity score <sup>c</sup>      |                      |                          |         |
| 0  | 1568 (23.9)          | 1729 (26.35)             | <.001   |
| 1-3  | 3260 (49.68)         | 3554 (54.16)             |         |
| ≥4   | 1734 (26.42)         | 1279 (19.49)             |         |
| Any reason outpatient visits,                |                      |                          |         |
| 0-10   | 1176 (17.92)         | 2089 (31.83)             | <.001   |
| 11-20  | 1269 (19.34)         | 1614 (24.6)              |         |
| 21-30  | 1140 (17.37)         | 1131 (17.24)             |         |
| ≥31  | 2977 (45.37)         | 1728 (26.33)             |         |

<sup>a</sup> 1US \$ = 32.1 New Taiwan Dollars (NTD) in 2008.

<sup>b</sup> ICD-9: Pancreatic disorder (577.X), alcohol-related disease (291,303.0,303.9,305.0,571.0,571.1,571.2,571.3), drug-dependent (304.XX), schizophrenia (295.XX), depressive disorder (296.2X, 296.3X, 300.4, 311), bipolar

disorder(296.0, 296.4, 296.5, 296.6, 296.7, 296.80, 296.89), anxiety disorder(300.0, 300.01, 300.02, 300.2, 300.21, 300.23, 300.3).

<sup>c</sup> All medical claims before index date.

<sup>d</sup> Summation past one year of index date.

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Table 2. Association between disease of pancreas and suicide in a population-based case-control study <sup>a</sup> Taiwan, 2002-2010.

| Variable   | Unadjusted analysis    |         | Adjusted analysis model 1 <sup>e</sup> |         | Adjusted analysis model 2 <sup>f</sup> |         |
|--|------------------------|---------|--|---------|--|---------|
|  | Odds-ratio<br>(95% CI) | P value | Odds-ratio<br>(95% CI)                 | P value | Odds-ratio<br>(95% CI)                 | P value |
| Medical and mental diseases,<br>yes vs no        |                        |         |  |         |  |         |
| Pancreatic disorder <sup>b</sup>                 | 2.66 (2.08-3.38)       | <.001   | 2.67 (2.02-3.54)                       | <.001   | 1.60 (1.19-2.17)                       | 0.002   |
| Alcohol-related disease                          | 3.44 (2.97-3.99)       | <.001   |  |         | 3.35 (2.81-4.00)                       | <.001   |
| Drug-dependent                                   | 4.33 (3.10-6.03)       | <.001   | 4.94 (3.35-7.30)                       | <.001   | 5.23 (3.52-7.77)                       | <.001   |
| Schizophrenia                                    | 3.83 (3.18-4.61)       | <.001   | 4.18 (3.38-5.17)                       | <.001   | 4.22 (3.39-5.24)                       | <.001   |
| Depression disorder                              | 5.87 (5.29-6.51)       | <.001   | 5.05 (4.53-5.64)                       | <.001   | 5.05 (4.51-5.64)                       | <.001   |
| Bipolar disorder                                 | 5.27 (4.09-6.79)       | <.001   | 2.96 (2.21-3.98)                       | <.001   | 2.78 (2.06-3.74)                       | <.001   |
| Anxiety disorder                                 | 1.45 (1.34-1.56)       | <.001   | 1.11 (1.01-1.22)                       | 0.029   | 1.17 (1.07-1.29)                       | 0.001   |
| Charlson comorbidity score <sup>c</sup>          |                        |         |  |         |  |         |
| 0  | 1.00 [reference]       |         | 1.00 [reference]                       |         | 1.00 [reference]                       |         |
| 1-3  | 1.05 (0.97-1.15)       | 0.241   | 0.92 (0.83-1.02)                       | 0.124   | 0.88 (0.79-0.98)                       | 0.025   |
| ≥4   | 1.69 (1.51-1.89)       | <.001   | 1.20 (1.04-1.38)                       | 0.012   | 1.10 (0.95-1.27)                       | 0.195   |
| Any reason outpatient visits, times <sup>d</sup> |                        |         |  |         |  |         |
| 0-10   | 1.00 [reference]       |         | 1.00 [reference]                       |         | 1.00 [reference]                       |         |
| 11-20  | 1.51 (1.36-1.68)       | <.001   | 1.33 (1.17-1.50)                       | <.001   | 1.35 (1.19-1.53)                       | <.001   |
| 21-30  | 2.05 (1.82-2.30)       | <.001   | 1.58 (1.38-1.81)                       | <.001   | 1.59 (1.39-1.83)                       | <.001   |
| ≥31  | 3.86 (3.46-4.30)       | <.001   | 2.62 (2.31-2.98)                       | <.001   | 2.70 (2.38-3.08)                       | <.001   |

<sup>a</sup> Exact matching by sex, age, residence, insurance premium.

<sup>b</sup> ICD-9: Pancreatic disorder (577.X).

<sup>c</sup> All medical claims before index date.

<sup>d</sup> Summation past one year of index date.

<sup>e</sup> Adjusted by drug-dependent (304.XX), schizophrenia (295.XX), depressive disorder (296.2X, 296.3X, 300.4, 311), bipolar disorder (296.0, 296.4, 296.5, 296.6, 296.7, 296.80, 296.89), anxiety disorder (300.0, 300.01, 300.02, 300.2, 300.21, 300.23, 300.3), Charlson comorbidity score and any reason outpatient visits

<sup>f</sup> Model 1+alcohol-related disease (291, 303.0, 303.9, 305.0, 571.0, 571.1, 571.2, 571.3),

CI: Confidence Interval.

Table 3. Stratified analyses of association between disease of pancreas and suicide in a population-based case-control study <sup>a</sup>, Taiwan, 2002-2010.

| Subgroup   | Unadjusted analysis                  |         | Adjusted analysis model 1 <sup>b</sup> |         | Adjusted analysis model 2 <sup>c</sup> |         |
|------------|--------------------------------------|---------|--|---------|--|---------|
|            | Odds-ratio<br>(95% CI <sup>d</sup> ) | P value | Odds-ratio<br>(95% CI <sup>d</sup> )   | P value | Odds-ratio<br>(95% CI <sup>d</sup> )   | P value |
| Total      | 2.66 (2.08-3.38)                     | <.001   | 2.67 (2.02-3.54)                       | <.001   | 1.60 (1.19-2.17)                       | 0.002   |
| Male       | 2.65 (2.03-3.46)                     | <.001   | 2.59 (1.92-3.51)                       | <.001   | 1.46 (1.05-2.02)                       | 0.024   |
| Female     | 2.66 (1.47-4.82)                     | 0.001   | 2.60 (1.29-5.25)                       | <.001   | 2.32 (1.13-4.77)                       | 0.022   |
| Aged 15-44 | 3.22 (2.22-4.65)                     | <.001   | 3.63 (2.35-5.61)                       | <.001   | 1.74 (1.07-2.84)                       | 0.026   |
| Aged 45-64 | 2.53 (1.68-3.81)                     | <.001   | 2.25 (1.40-3.62)                       | <.001   | 1.35 (0.82-2.24)                       | 0.239   |
| Aged ≥65   | 1.86 (1.09-3.16)                     | 0.022   | 1.93 (1.06-3.53)                       | 0.032   | 1.70 (0.92-3.12)                       | 0.089   |

<sup>a</sup> Exact matching by sex, age, residence, insurance premium.

<sup>b</sup> Adjusted by drug-dependent (304.XX), schizophrenia (295.XX), depressive disorder (296.2X, 296.3X, 300.4, 311), bipolar disorder (296.0, 296.4, 296.5, 296.6, 296.7, 296.80, 296.89), anxiety disorder (300.0, 300.01, 300.02, 300.2, 300.21, 300.23, 300.3), Charlson comorbidity score and any reason outpatient visits

<sup>c</sup> Model 1+alcohol-related disease (291, 303.0, 303.9, 305.0, 571.0, 571.1, 571.2, 571.3),

CI: Confidence Interval.